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BACTERIAL CAUSATIVE AGENTS OF URINARY TRACT INFECTIONS (UTIs) AND THEIR ANTIBIOTIC SENSITIVITY PATTERN IN KHARTOUM, SUDAN

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ABSTRACT

Background: Urinary Tract Infections (UTIs) are amongst the most prevalent bacterial infections seen in clinical practice particularly in developing countries. **The objective of this study was** to determine the etiological bacterial pathogens of the UTI and their sensitivity to antibiotics. **Methodology:** a cross sectional study carried out in Om Durman Islamic University microbiology laboratory, in Om Durman (Sudan) from March to May 2012, A total of 50 urine samples were collected and subjected to bacteriological identification tests and sensitivity tests. **Results**: Out of 50 urine samples 45 (90%) provided positive growth. *Escherichia coli* was the most common (31.1%) followed by *Klebsiella spp* (13.3%) ,*Staphylococcus aureus* (11.2%), *Proteus spp* and *Pseudomonas aeroginosa* (8.9%), *Salmonellae spp* and *Enterococcus faecalis* (6.7%), *Enterobacter* and *Staphylococcus epidermidis* (4.4%) and *Staphylococcus saprophyticus* and *Citrobacter*(2.2%). The highest susceptible age to UTI was 41 -50 years (35%) followed by 31-40 (28%), 21-30 (18%), >50 years (14%) and 10-20 years (6%). More cases were observed in females except in age group >50 years. Norfloxacin had the least resistance followed by Ciprofloxacin, Cephalexin and Co-Timoxazole. *E. coli*

found to be highly resistant to Cephalexin, Ciprofloxacin and Co-Trimoxazole(42.9%). Whilst *Klebsiella spp* showed highly resistance (100%) to Cephalexin. Whereas *Staphylococcus auerus* showed highest sensitivity (100%) to used antibiotics. **Conclusion:** The results show that the *E.coli* was the most frequent causative agent in UTIs and antimicrobial resistance patterns of the causes of UTI are highly variable and continuous surveillance of trends in resistance patterns of uropathogens is important. In conclusion; we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal or even national guidelines.

KEYWORDS: Urinary Tract Infections (UTIs), Antibiotic Susceptibility, Anti Microbial agents, Bacteria, *E.coli*.

INTRODUCTION

The urinary tract contains the urethra, urinary bladder, ureters, and kidneys.[1] Urinary tract infections (UTIs) are among the most common bacterial infectious diseases encountered in clinical practice, and account for significant morbidity and high medical costs. When it affects the lower urinary tract it is known as a simple cystitis (a bladder infection). Alternatively, it may involve the upper urinary tract, in which case it is known as pyelonephritis.[2]

UTIs can be grouped into asymptomatic bacteriuria or depending on the site of infection: urethritis, cystitis, or pyelonephritis, and by severity (simple, uncomplicated, complicated, recurrent, or relapsing).[3]

UTIs are more common in women than men.[1] In children when a urinary tract infection is associated with a fever, it is deemed to be an upper urinary tract infection.[4] The most common symptoms are durning with urination and having to urinate frequently and significant pain.[5] In young children, the only symptom of a urinary tract infection (UTI) may be a fever.[6]

By far the most common cause (~80%) of UTIs is the gram negative bacteria *Escherichia coli* (*E.coli*). The specific strains that usually cause UTIs are the uropathogenic *E. coli* (UPEC) [7,8] with *Staphylococcus saprophyticus* being the cause in 5-10%. Rarely they may be due to viral or fungal infections.[9] Other bacterial causes UTIs include: *Klebsiella*,

Proteus, *Pseudomonas* and *Enterobacter*. [4] Urinary tract infections due to *Staphylococcus aureus* typically occurs secondary to blood born infections[1]. Urinary tract infections are the problems that are faced by millions of people every year.[10]

Early initiation of antibiotic treatment following suspicion of UTI is thought to decrease the risk of kidney scarring.[11] Early and appropriate treatment during the first 24 hours after onset of symptoms however may diminish the likelihood of kidney involvement during the acute phase of the infection.[12] Delayed treatment may lead to complications such systemic sepsis and abscess formation.[13]

Antimicrobial resistance of uropathogens is increasing worldwide.[29] Especially resistance of *E. coli* and other Enterobacteriaceae. In addition Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin resistant *Enterococcus spp*. They play an important role in hygienic issues in patients.[14] *E.coli* resistance to B-lactam antibiotics as high as 37.7% and to Trimethoprim–Sulfamethoxazole as 21.3%[15], thus making these agents inadequate as first line treatment for UTI[16]. The final choice of antibiotic should be based on pathogen identification and sensitivity test from urine culture.[17] Cephalosporin and Amoxicillin-Clavulanic acid are the oral antibiotics most often used.[18] The choice of intravenous antibodies is usually a Cephalosporin combined with an Aminoglycoside. Although, no particular antibiotic choice has been shown to be superior.[19, 20] However, it must be noted that the best method of directing antibiotic choice will be based in resistance patterns in a given institution or region. However, following the increasing of *E. coli* and other bacteria to first line antibiotics there has been a rise in the rate of UTIs.[21] As example; the healthcare costs from UTIs in the U.S. is estimated to be over 2.3 billion dollars per year.[22]

Objectives

1. To determine the etiological bacterial pathogens of the UTIs.
2. To determine the antibiotic sensitivity pattern of isolated bacteria.

MATERIALS AND METHODS

Study area: A cross sectional study was conduct from March to May 2012 to evaluate UTIs in Khartoum state (Sudan).

Study location: Samples were collected from patients from National Centre for Radiotherapy and Nuclear Medicine.

Statistical analysis: The obtain results were statistically analyze using prevalence by Excel.

Laboratory work: based on Monica Cheesbrough 2006.[23]

A 50 specimens of clean catch mid-stream urine were collected from patient in sterile, screw capped, leaf proof disposable plastic container, each specimen had been kept in ice for less than one hour till reaching the laboratory.

Isolation of bacteria: Specimens were cultured by inoculation on general, enriched and selective agar and incubated in an atmosphere containing 5% carbon dioxide. Cultures were classified according to the standard criteria used in laboratory; any count of 10^5/ml of Gram negative pathogen, or Gram positive pathogen in pure growth considered as **Positive** (infection). Currently, bacteria from urine are identified by using identification tests include biochemical tests such as Motility, Indole, Urease medium. Also other tests were conducted include citrate utilization test, oxidase test and carbohydrate fermentation tests using TSI and KIA.

Antimicrobial susceptibility testing: Antibiotic sensitivity test was performed by disc diffusion method (Kirby-Bauer's technique) using commercially available discs (Hi Media, India), and the results were recorded following the instruction of manufacturer. These test discs used included: Cotrimoxazole (1.25/23.75 mcg), Cephalexin (30 mcg), Ciprofloxacin (5mcg) and Norfloxacin (10 mcg).

RESULTS

Bacterial etiology of UTIs in patients admit in National centre for Radiotherapy and Nuclear Medicine (Al Zara hospital) - Khartoum state (Sudan) (during the study period) was determined.

The result of this study revealed that positive specimens which showed positive bacterial growth were 90 %(n=45). However, 10% (n=5) showed negative growth, but the patients had urinary tract infection symptoms. This is may be due to other causative agents not detected by this study, vide table.[1]

Table (1): The distribution of positive and negative urine samples

Item	Number	%
Positive growth	45	90
Negative growth	5	10
Total of samples	50	100

The present study results determine that in under test samples the most frequency belongs to *E. coli* bacterium (31.1% of the whole sample positive) and in the next class *Klebsiella spp* (13.3%) and *Staphylococcus aureus (*11.2*%* of the whole sample positive) which all are detailed in table(2)

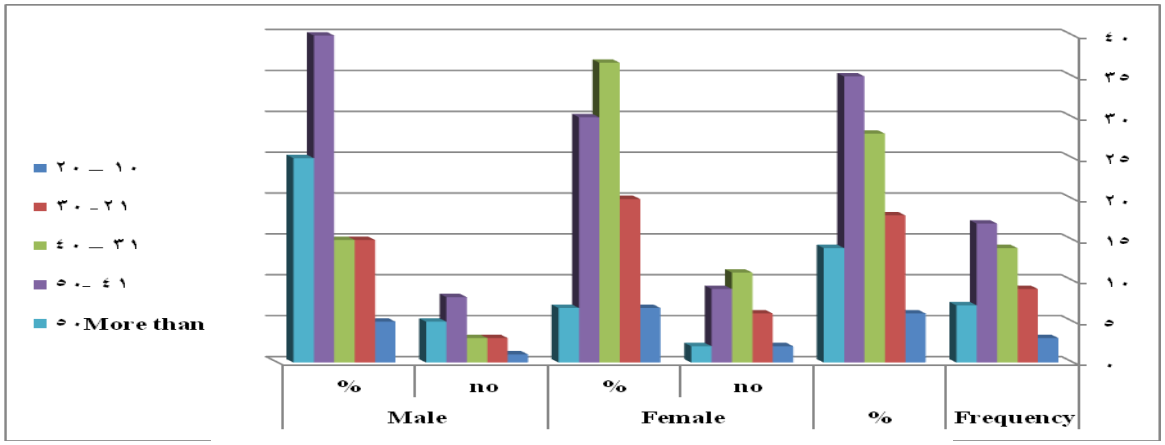
Table (2) Frequency and distribution of isolated pathogens

Organism	Frequency	Percentage %
Escherichia coli	14	31.1
Klebsiella spp	6	13.3
Staphlococcus aureus	5	11.2
Proteus spp	4	8.9
Pseudomonas aeroginosa	4	8.9
Enterococcus faecalis	3	6.7
Salmonellae spp	3	6.7
Staphlococcus epidermidis	2	4.4
Enterobacter	2	4.4
Staphylococcus saprophyticus	1	2.2
Citrobacter	1	2.2
Total	**45**	**100**

The highest susceptible age group of patients to UTI was 41 -50 years (34%) followed by 31-40 years (28%), 21-30 years (18%), more than 50 years (14%) and 10-20 years (6%). Comparatively, however, more cases of UTI were observed in females than in males in all age groups except in age group more than 50 years (Table: 3).

Table (3): Prevalence of UTI in different age groups and genders

Age range	Frequency	%	Female		Male	
			no	%	no	%
10 – 20	3	6%	2	66.7	1	33.3
21– 30	9	18%	6	66.7	3	33.3
31 – 40	14	28%	11	78.6	3	21.4
41 – 50	17	34%	9	52.9	8	47.1
More than 50	7	14%	2	28.6	5	71.4
Total	50	100%	30		20	



Prevalence of UTI in different age groups and genders

The antimicrobial potency and spectrum of four selected antimicrobial agents (common used in Sudan), against the UTIs pathogens recorded in the study are summarized in table (4). Norfloxacin had the least resistance followed by Ciprofloxacin, Cephalexin and Co-Trimoxazole respectively.

The sensitivity pattern of bacterial isolates against a number of antibiotics revealed that *E. coli* was the highest bacteria isolated from urinary tract infection exhibited various rate of sensitivity to all used antibiotics (Cephalexin, Ciprofloxacin, Norfloxacin and Co-Timoxazole) as shown in table (4), followed by *Staphylococcus auerus* which showed highest sensitivity(100%) to all used antibiotic (Table 4).

Table (4) Illustrate antibiotic susceptibility test: sensitivity of isolated bacteria to used antibiotics

Name of isolated bacteria	Cephalexin		Ciprofloxacin		Norfloxacin		Co-Timoxazole	
	S (n) %	R (n)%	S (n)%	R (n)%	S (n)%	R (n)%	S (n)%	R (n)%
Escherichia coli	(8)57.1%	(6)42.9%	(8)57.1%	(6)42.9%	(14)100%	(0)	(8)57.1%	(6)42.9%
Klebsiella SPP	(6)100%	0	(6)100%	(0)	(6)100%	(0)	(5)83.3%	(1)16.7%
Staphlococcus aureus	(5)100%	(0)	(5)100%	(0)	(5)100%	(00	(5)100%	(0)
Proteus spp	(4)100%	(0)	(4)100%	(0)	(4)100%	(0)	(0)	(4)100%
Pseudomonas aeroginosa	(4)100%	(0)	(4)100%	(0)	(4)100%	(0)	(4)100%	(0)
Enterococcus faecalis	(3)100%	(0)	(3)100%	(0)	(3)100%	(0)	(3)100%	(0)
Salmonellae spp	(3)100%	(0)	(3)100%	(0)	(3)100%	(0)	(3)100%	(0)
Staphlococcus epidermidis	(2)100%	(0)	(2)100%	(0)	(2)100%	(0)	(0)	(2)100%
Enterobacter	(2)100%	(0)	(2)100%	(0)	(2)100%	(0)	(0)	(2)100%
Staphlococcus saprophyticus	(1)100%	(0)	(1)100%	(0)	(1)100%	(0)	(1)100%	(0)
Citrobacter	(1)100%	(0)	(1)100%	(0)	(1)100%	(0)	(1)100%	(0)

DISCUSSION

Urinary tract infections are common conditions worldwide, particularly in developing countries, and the pattern of antimicrobial resistance varies in different regions. This study evaluate the relationships between sex, age, and isolated bacterial agents and antibiotic resistance of UTIs.

This study provides valuable data to compare and monitor the status of antimicrobial resistance among uropathogens to improve efficient empirical treatment. Increasing antimicrobial resistance has been documented globally.[24, 25]

The study showed a high prevalence of UTIs in females n=30 (60%) than in males n=20 (40%) which correlates with other findings, revealed that the frequency of UTIs is greater in females as compared to males.[26, 27] and [30] The reason behind this high prevalence of UTIs in females is due to close proximity of the urethral meatus to the anus, shorter urethra, sexual intercourse, incontinence, and bad toilet.[31]

The occurrence of UTIs recorded among the 41-50 years, 34% compared to young age patients (21-30 years, 18%; 10-20 years, 6%) and middle-age patients (31-40 years, 28%) in this study partly similar to the studies done in Kuwait [32] and Nigeria [29,33] in which the highest incidence of UTIs was recorded among the age group 20 to 50 years (63.4 and 74.7%, resp.), and lowest among the age group >50 years (13.3 and 10.3%, resp.). However, the results agree with the study done in Japan with a 20-year period in which a trend of increasing complicated UTIs was reported in elderly patients.[34] The study proved that, the elderly males (≥50 years) had a higher incidence of UTIs (71.4%) when compared with the elderly females (28.6%). This finding is similar to a study conducted at a tertiary care hospital in Jaipur, Rajasthan, India.[30] The main cause behind this increasing incidence of UTI with advancing age in males is due to prostate enlargement and neurogenic bladder.[35] This factor is also reported by other authors whose studies showed that the prostate disease in males is responsible for the increase in incidence of UTI and decrease in female: male ratio in patients above 50 years.[36] Females of the age group 31 - 40years were found more susceptible (78.6) to UTI followed by 21-30 years (66.7) ,41-50 years (52.9%), 10-20 years and ≥50 years (28.6%). These findings correlate with other reports which showed that females are more prone to UTIs than males during adolescence and adulthood.[37, 38, 39, 40] The highest incidence of UTIs among female to male ratio was found in the age group of 31 - 40years (3.7 : 1) followed by10–20 years and 21- 30 years (2 : 1), 41 -50years (1.1 : 1), and

≥50 years (0.4 : 1). These findings differ from other reports[41, 42] which stated a lower female to male ratio in neonates and young children. The prevalence rate of UTI in boys depends on many factors including congenital malformations and uncircumcised genitalia which are often contaminated.[41]

A variety of Enteropathogenic bacteria are known to cause UTI worldwide. *E. coli* being the predominant aetiological agent in community practice. Other bacterial agents include species of *Klebsiella, Enterobacter, Proteus, Pseudomonas, Staphylococcus, Streptococcus* and *Enterococcus faecalis.*[35, 44] In this study, *E.coli* and *Klebsiella spp* represents (31.1%), (13.3%)respectively, both of them were recorded as the predominant bacteria causes UTIs, this finding similar to the study done by.[43, 44, and 45] Moreover as is evident from the results, this study demonstrated *E. coli* to be the predominant aetiological agent amongst the gram negative bacilli and *Staphylococcus aureus* amongst gram positive bacteria as the causative agents of UTIs. These findings are similar to other studies conducted by.[46, 47, and 48]

Other isolated bacteria from UTI cases in this study was *Staphylococcus aureus* (11.2%), *P. aeruginosa* (8.9%), *Proteus spp*. (8.9%), *Enterococcus faecalis* (6.7%), *Salmonellae spp*. (6.7%), *S. epidermidis* (4.4%), *Enterobacter spp*. (4.4%), *S. saprophyticus* (2.2) and Citrobacter (2.2). These findings were not correlate with other reports in which *P. aeruginosa* was reported as the second most common bacterial isolate in UTI studies in India[40] and Lafia, Nigeria[39] however, these results correlates with others in which *Klebsiella spp* was reported as the second most frequently isolated organism in UTIs.[49,50]

It must be borne in mind, that the variations in antimicrobial susceptibility in different countries and within states in our country, may depend upon the easy availability of antimicrobial drugs over the counter. Cephalexin, Ciprofloxacin, Norfloxacin and Co-Trimoxazoleare very commonly used over the counter drugs for UTIs treatment in our country Also various reports indicate that the level of resistance in different parts of the world varies from 18 to 50 percent which is probably associated with the consumption rate of this drug.[51, 52]

The results of this study suggest that Norfloxacin had effectiveness(100%) against all isolated bacteria in this study, followed by Ciprofloxacin, the highest sensitivity belongs to all most isolated bacteria (100%), with less sensitivity against *E. coli* (57.1%) this was partially agree

with report stated by Gupta et al [50], Gales et al[51], Yousefi et al and [52] Goettsch et al[53]. The study reflect, that Cephalexin and Co-Trimoxazolerespectively. *E.coli* exhibited (42.9%) resistant to Cephalexin, Ciprofloxacin and Co-Timoxazole. Whereas Klebsiella spp showed (100%) resistance to Cephalexin and (83.3%) to Co-Timoxazole, furthermore, *Proteus spp, Staphylococcus epidermidis* and *Enterobacter* were showed resistance (100%) to Co-Timoxazole.

CONCLUSION

The study conclude that the *E.coli* was the most frequent causative agent in UTIs and antimicrobial resistance patterns of the causes of UTIs are highly variable and continuous surveillance of trends in resistance patterns of uropathogens is important.

In conclusion; we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organisms and antibiotic sensitivities rather than on universal or even national guidelines.

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